Year 2

Endocrine and genitourinary module

I want to get pregnant

Basic Science Principlesfor Clinical Reasoning

1- **Critical thinking**

2- Introduction to **common forms of disease**

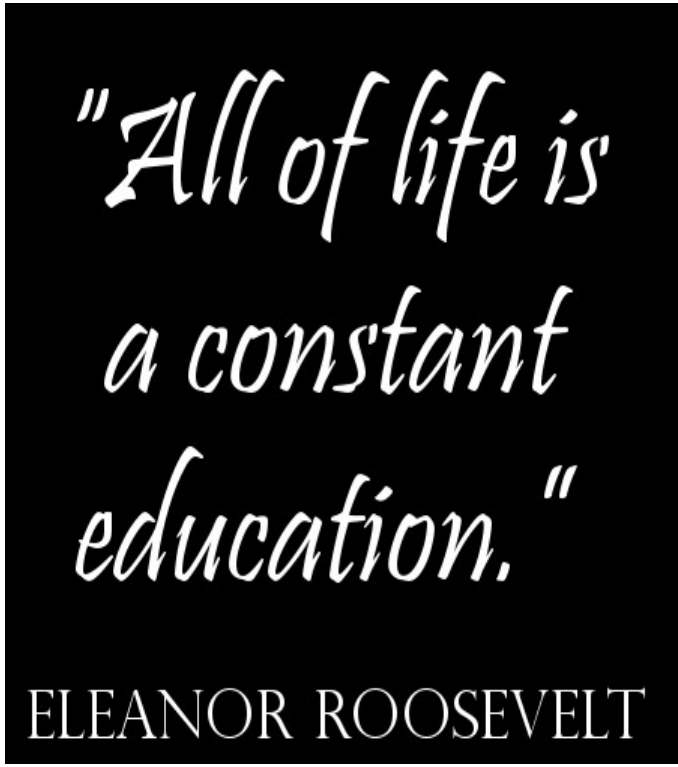
3- **How basic sciences help understanding**

4- **Respect patient's complaint** & **symptoms**

5- **Create questions**

6- **Problem solving**

7- **Building teams** **Interpersonal skills**



Dealing with

Case co-ordinator

Prof. Dr. Alaa Elguindy, Manal Hassan, Lamiaa Foad, Walid Kafafi

I want to get pregnant

Laila is a 37-year-old female. She is married to Roshdy who is 37-years-old. They were married 7 years ago. They presented to the infertility clinic with the complaint of inability to conceive for the **last 2 years**.

Laila has a 5-years-old daughter. Laila reports good health and no problems in conceiving her previous pregnancy or in the vaginal delivery of her daughter.

I want to get pregnant

Roshdy has no medical problems or past surgery. He works as a long-distance **truck driver** and is on the road 1-2 weeks each month. He smokes a pack of cigarettes a day since age 18.

He occasionally uses **amphetamines** to stay awake while driving at night.

The couple has sexual intercourse 3-5 times per week when he is at home.

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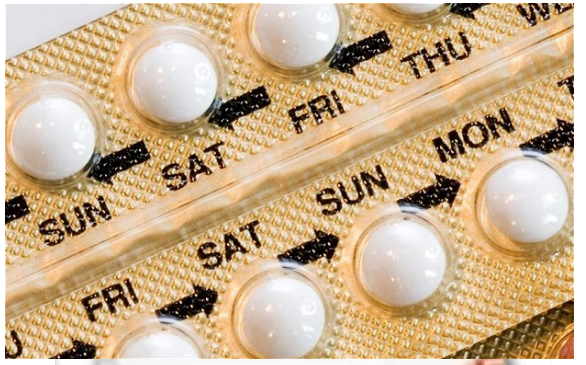
The doctor asked Laila about her **menstrual cycle** and whether she has taken any **contraception**.



Laila said that she used **birth control pills** until 2 years ago. The couple has been trying to conceive since then and report a high degree of stress related to their lack of success.

She reported that her periods were regular on the birth control pills, but has been irregular since she discontinued taking them. She reports having **periods every 5-7 weeks**.

I want to get pregnant

Past history is remarkable only for mild depression. She has been taking **Imipramine** for the last year.

Laila has **no** history of **sexual transmitted diseases** and **no abnormal Paps**.

No smoking, no alcohol or other drug intake.

She has had no surgery.

The doctor asked her about any discharge from the breast. Laila said that she occasionally has transparent or whitish **breast discharge**

I want to get pregnant

Examination

Laila is 160cm in height and weighs 90 kilos.
Vital signs: within normal

Breast examination: revealed no tenderness or masses, but **bilateral galactorrhea on compression of the areola**.

Pelvic exam reveals normal genitalia, **well-estrogenized vaginal vault mucosa** and **cervical mucus** consistent with the proliferative phase.

The uterus is **anteflexed** and normal in size without masses or tenderness.

Discussion

Laila and Roshdy who are 37 years old presented to the infertility clinic with the complaint of inability to conceive for the last **2 years**.

1- Is this duration significant?

Explain

Definition of infertility

1. No conception +
2. Regular sexual intercourse +
3. Unprotected sexual intercourse with No contraception
4. For One year

Types

1. **Primary infertility (never pregnant) = 1/3 of cases**

2. **Secondary infertility (Previous pregnancy) = 2/3 of cases**

- This duration is significant as this is a case of secondary infertility

- In secondary infertility the significant period of infertility reduced to 6 months not one year

Chances of conception

Half of those who do not conceive in the first year will do so in the second year
(cumulative pregnancy rate over 90%)

The chances of conceiving in any given menstrual cycle is less than 20%

2- List the couple’s problems

List the couple’s problems

Female problems

1. Oligomenrrhea
2. Galactorrhea (hyperprolactinemia)
3. Using antidepressant drugs
4. High BMI

Male problems

1. Occupational problems as a truck driver which affect spermatogensis
2. Using spermato-toxic drugs as amphetamine
3. Smoking

- **Sexual problems for both of them**
- **Absence of sexual intercourse for 2 weeks or more due to the nature of his occupation**

Laila and Roshdy reported good health with no problems with intercourse nor prior urogenital infections or exposure to sexually transmitted diseases STDs.

3- a. Why did the doctor ask about urogenital infections?

b. What are the common sexually transmitted diseases?

c. What other infections may affect fertility?

Factors affecting Fertility

STDs and Other Infections

- **Gonococci (causing gonorrhea) and Chlamydia trachomatis D-K (causing non-gonococcal urethritis) can lead to:**
  - **in women: cervicitis, salpingitis, and pelvic inflammatory disease (major cause of tubal infertility)**
  - **in men: urethritis, epididymitis, accessory gland infection**
- **Other infections that may affect fertility include:**
- **Mumps, leading to orchitis, may cause secondary testicular atrophy**
- **Tuberculosis, toxoplasmosis, malaria, schistosomiasis and leprosy**

Roshdy works as a long-distance **truck driver** and is on the road 1-2 weeks each month.

4- Is there a relation between occupation and male fertility?

Toxic Agents For spermatogenesis

The effect is dose related, and is reversible with many cases:

Occupational hazards:

- *Working with heavy metals:* battery workers, painters, welding processes.
- *Exposure to high temperatures*: Smelters.
- *Exposure to pesticides*.
- *Exposure to chemical toxic agents:* Textile industry, Plastic manufacture, Dry cleaning
- *Exposure to radioactive materials.*

Occupational hazards:

Unhealthy habits:

Unhealthy habits:

Heavy smoking.

Alcoholism.

Addiction e.g. cannabis.

Therapeutic agents:

He occasionally uses **amphetamines** to stay awake while driving at night.

5- Is the drug history important in Roshdy?

Drug history is important in this case

As some drugs affect fertility and this effect is reversible with most of them

1- Chemotherapeutic agents: these induce germinal epithelial aplasia

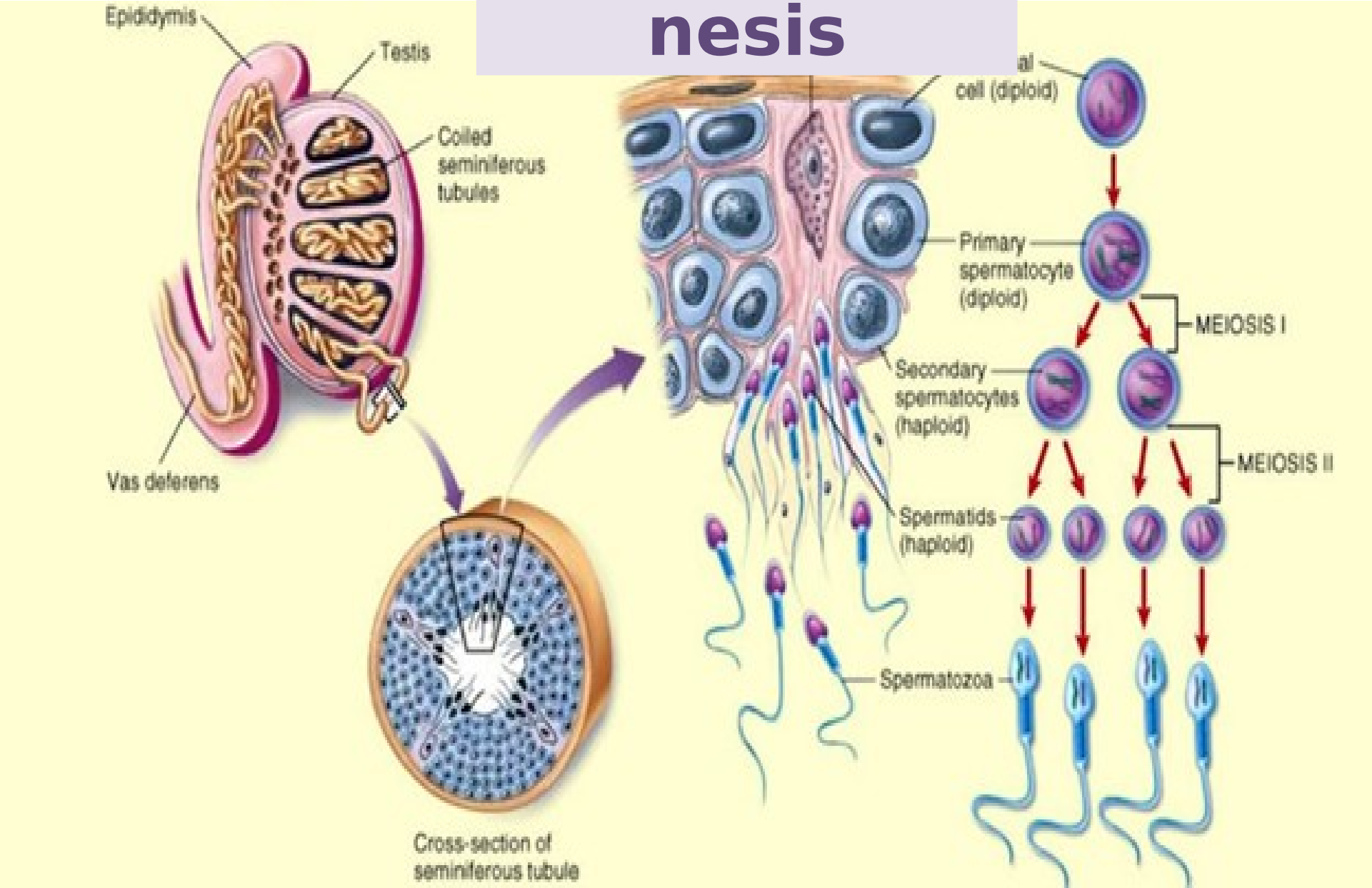
Methotrexate , cisplatin

2- Depression of spermatogenesis is possible with the following drugs:

spironolactone, ketoconazole , cimetidine , anti-malarial drugs, corticosteroids, salicylic acid derivatives, sulfasalazine, anabolic steroids, amphetamines,,

What are the steps of spermatogenesis and factors affecting it?

Spermatogenesis



Roshdy is on the road 1-2 weeks each month.

6- Interpret

Fertile Period in Female Sexual Cycle:

- ✓ The **ovum** remains viable and capable of being fertilized after it is expelled from the ovary probably no longer than 24 hours.
- ✓ The **sperm** remain fertile in the female reproductive tract for up to 5 days.
- ✓ Therefore, for fertilization to occur the sperm must be available soon after ovulation. Thus, sexual intercourse must occur ***between 4 and 5 days before ovulation up to a few hours after ovulation.***

Laila said that she used **birth control pills** until 2 years ago.

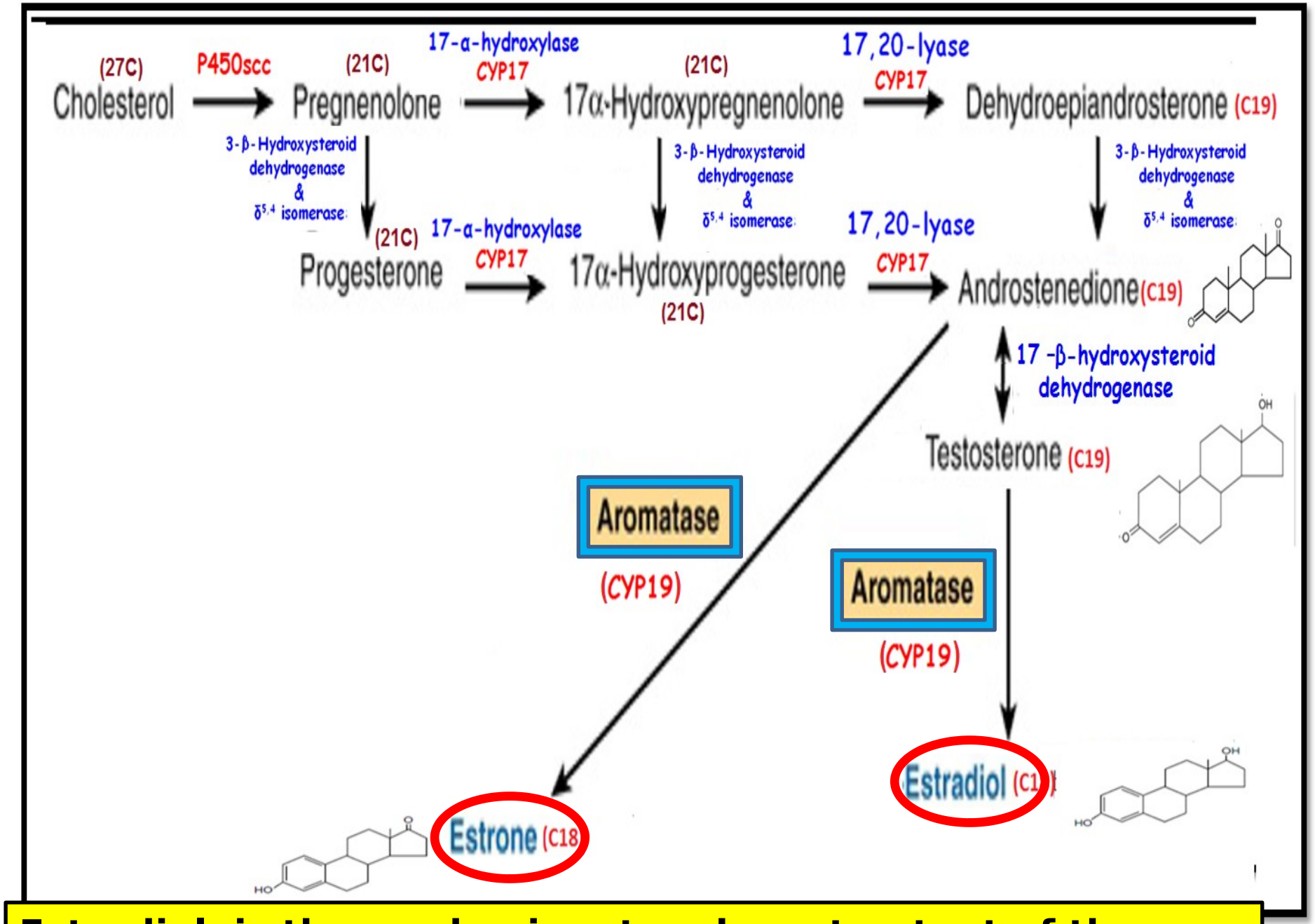
7- What is the nature of contraceptive pills?

1-Combined OCP: estrogen +progestins

2- Progestin only (mini-pill)

Contraceptive pills are hormonal in nature

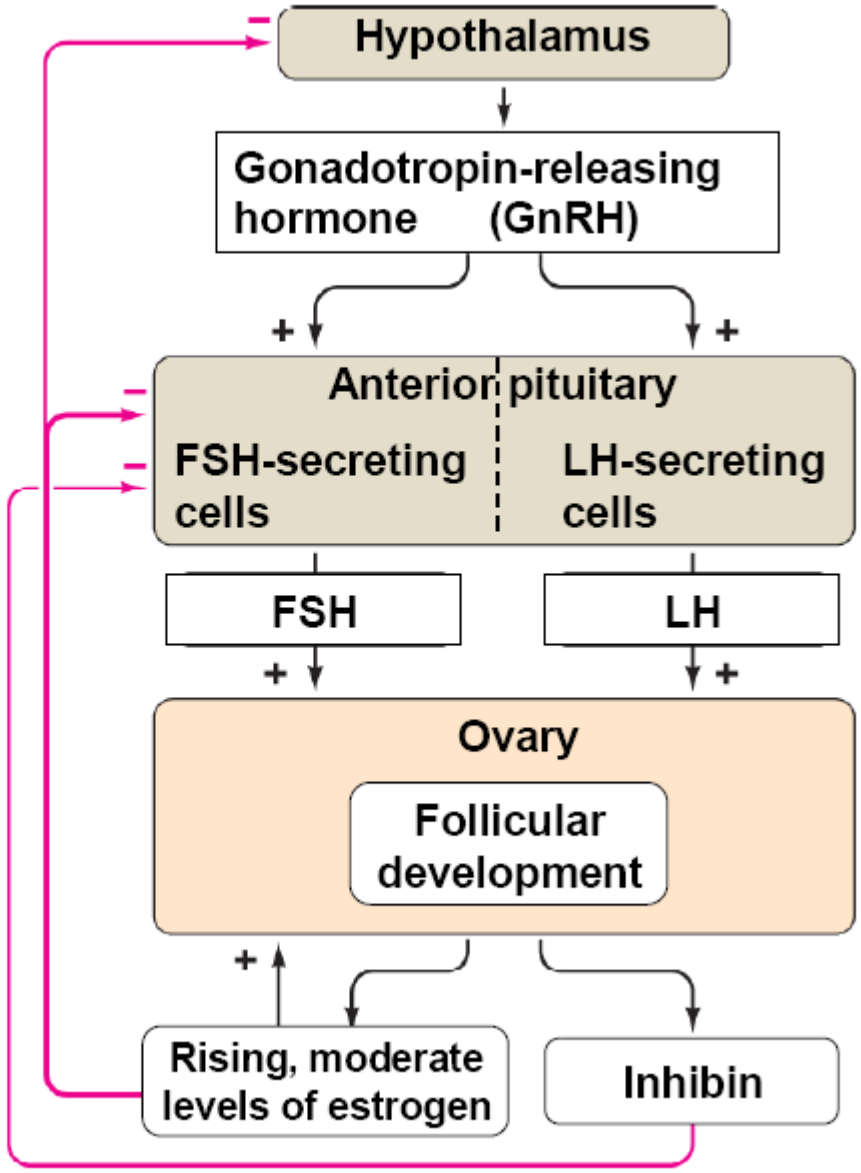
What hormones are produced by the ovary?
What are the steps of their synthesis ?



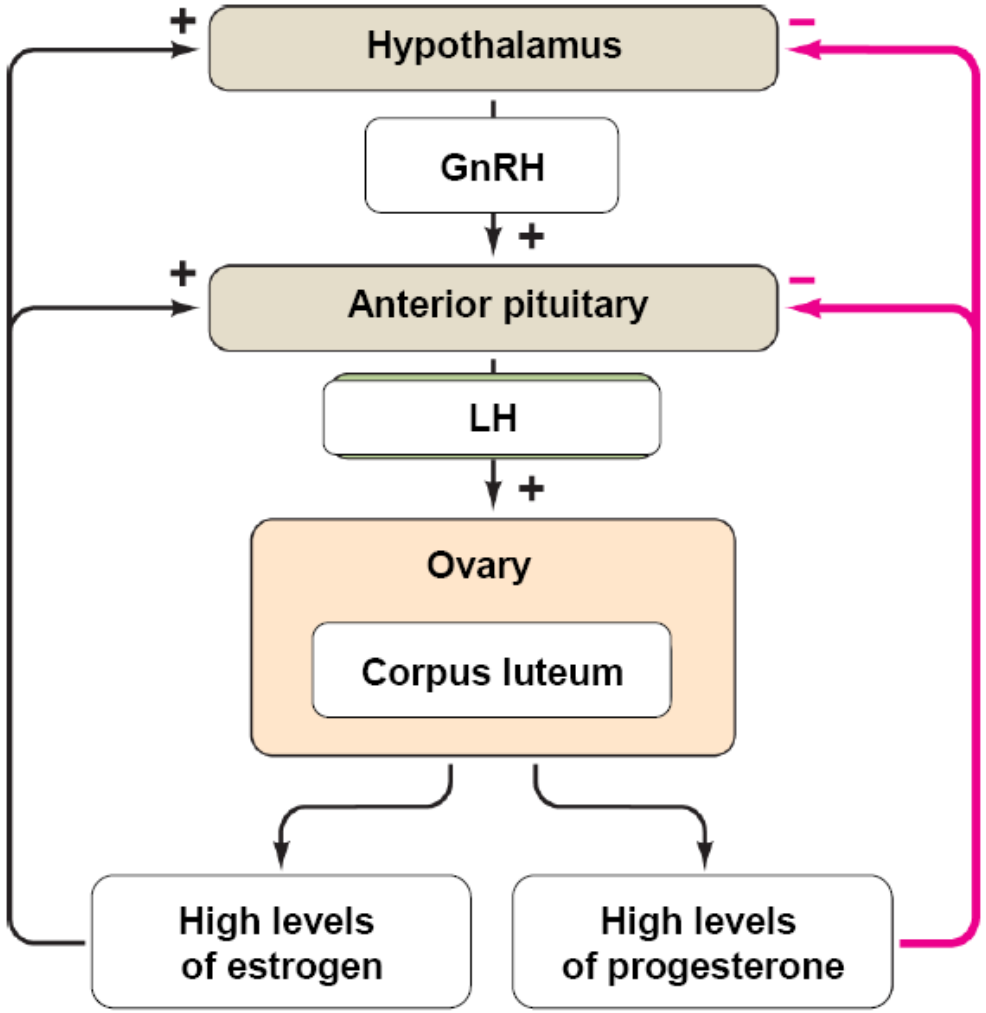
Estradiol, is the predominant and most potent of the ovarian estrogens

8- How could estrogen hormone act as a contraceptive?

Control of Ovarian hormones



During Follicular phase



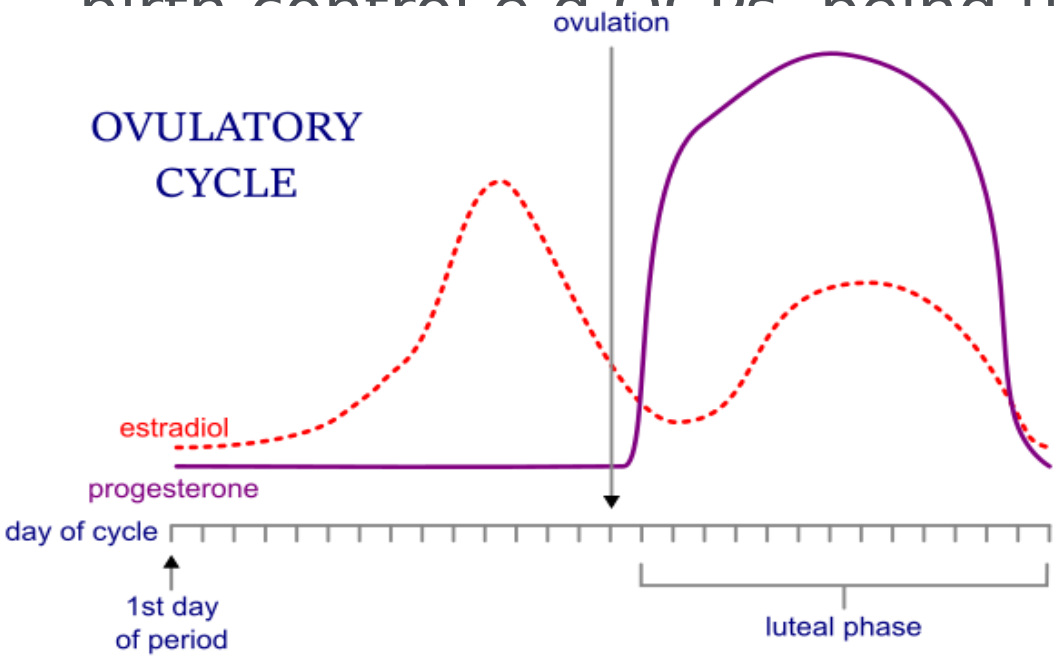
During Luteal phase

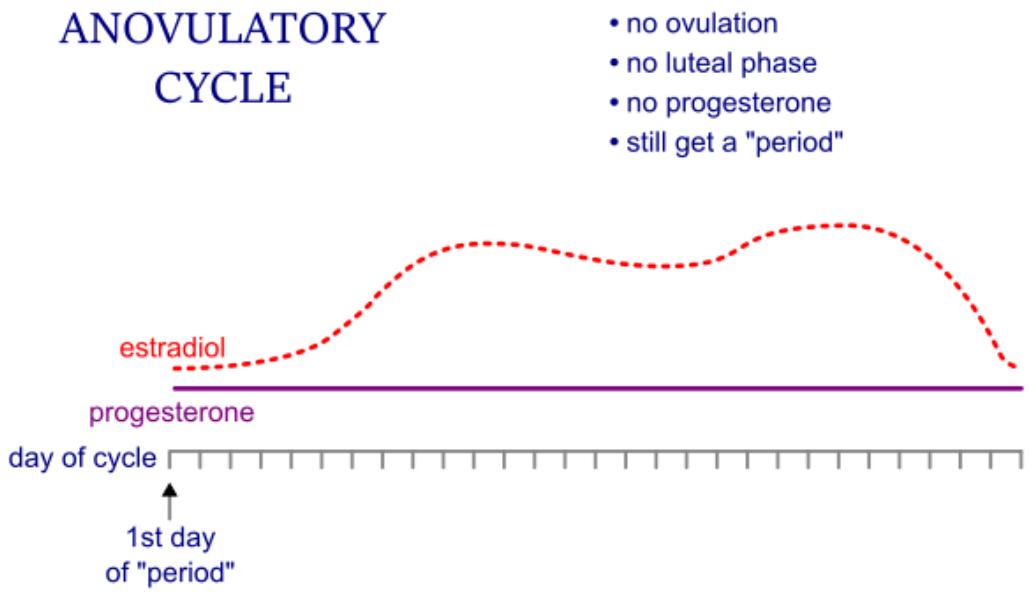
She reported that her periods were regular on the birth control pill, but has been irregular since she discontinued taking them. She reports having **periods every 6-7 weeks**.

Interpret

What are the possible causes of extended menses irregularity?

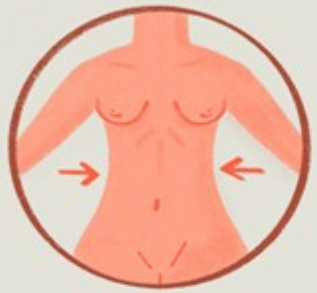
- ✓ This patient may have **anovulatory cycles** due to use of **OCPs.**
- ✓ Anovulatory cycles are menstrual cycles without ovulation due to insufficient LH surge.
- ✓ Anovulatory cycles are common for the first year after the onset of puberty, before the onset of the menopause, females using hormonal birth control e.g. OCPs, being underwei gnifican





Common Causes of Anovulation and Ovulatory Dysfunction

Polycystic ovarian syndrome (PCOS)



Too low body weight

Extreme exercise

Extremely high levels of stress

Hyperprolactinemia

Thyroid dysfunction (hyperthyroidism)

Perimenopause, or low ovarian reserves

Premature ovarian failure

9- What are the possible causes of extended menses irregularity in Laila?

The post pill amenorrhea period could extend up to 6 months and if more than this period there is probably another cause and the first cause to think about is hyperprolactinemia

She has been taking **Imipramine** for the last year.

Could drugs affect female fertility?

Imipramine is the least antidepressant drug affecting fertility compared to:

- **other antidepressants as SSRI**

or

- **antipsychotics as risperidone**

that increase serum prolactin level inhibit ovulation

Laila is 160cm in height and weighs 90 kilos.

What is Laila BMI?

What is its clinical significance?

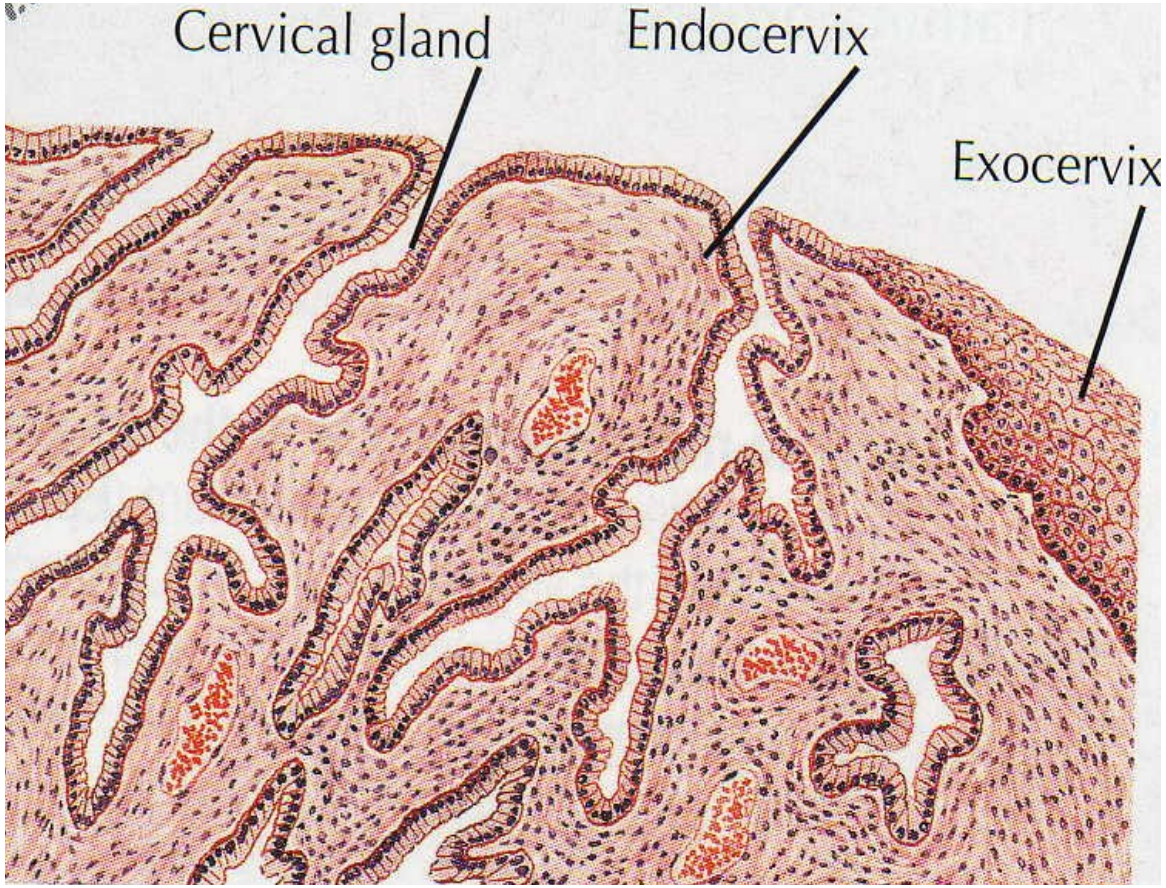
- High BMI may be associated with anovulation and conditions as polycystic ovarian syndrome

Pelvic exam reveals normal genitalia, **well-estrogenized vaginal vault mucosa** and **cervical mucus** consistent with the proliferative phase.

. What is meant by **well-estrogenized vaginal mucosa?**

What is the importance of cervical mucus?

Cervix

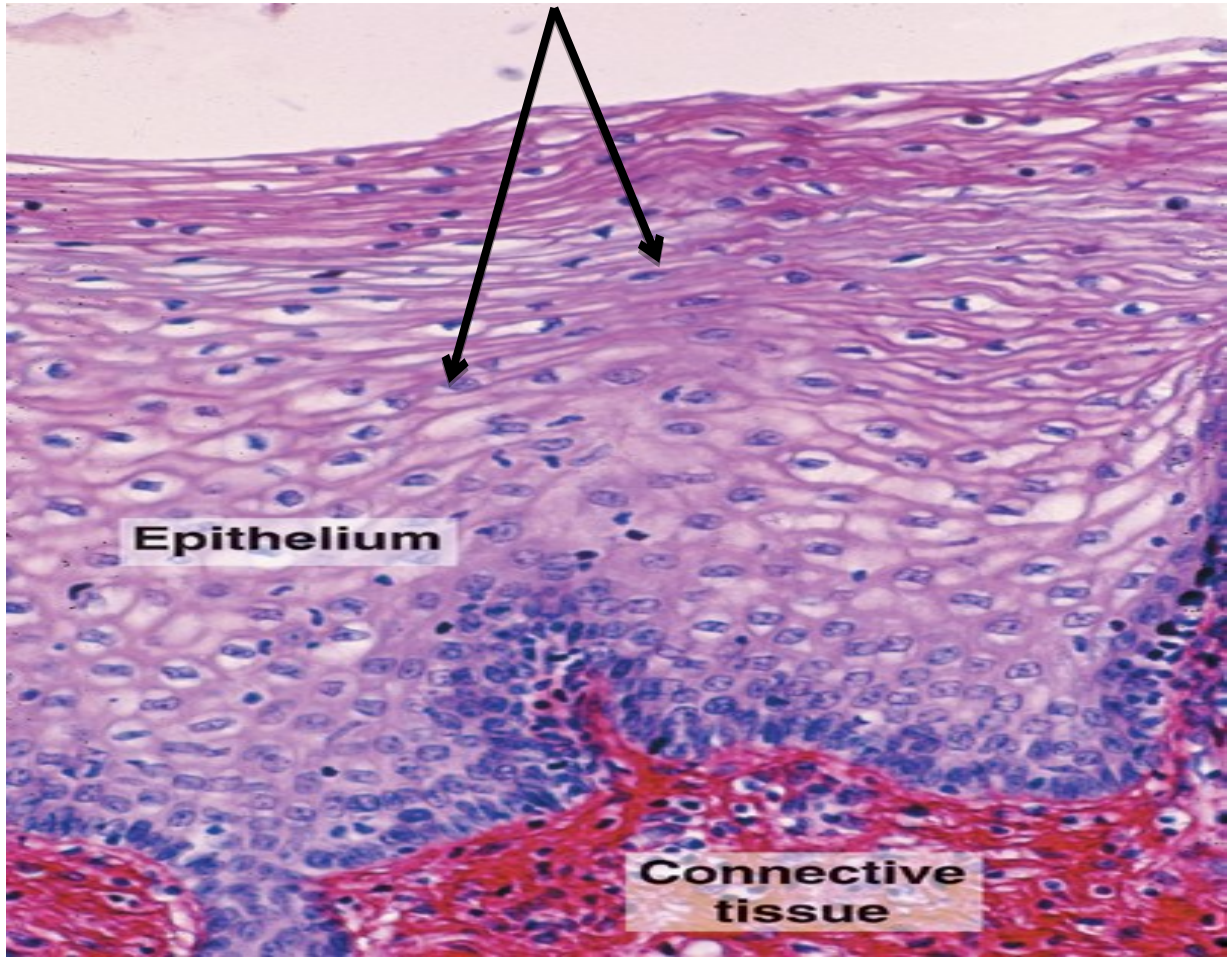


❑Cyclic changes of the cervix:

- **The cervical mucosa is not shed during menstruation, but cyclic changes occur in the amount and viscosity of the cervical secretion.**
- **Under effect of estrogen, cervical mucus is watery.**

Vagina

:Note
.Vacuolated epith



Under influence of estrogen:

- **↑ thickness of epithelium (multi-layered).**
- **↑ synthesis and storage of glycogen in superficial cells.**
- **Lamina propria is highly vascularized.**

What are the reproductive actions of estrogen and progesterone?

Biological Actions of Estrogens and Progesterone

Target Organ	Estrogen	Progesterone
Uterus	1. Endometrial thickening 2. Make cervical mucus thinner and more alkaline	1. Increasing vascularization of the endometrium during the luteal phase 2. Make cervical mucus more viscous
Vagina	1. More comified vaginal epithelium 2. Induce synthesis of pheromones' in vaginal secretion	1. Induces thick mucus secretions from the vaginal epithelium 2. Causes epithelium to thicken and become infiltrated with leukocytes
Breast	1. Promote growth and proliferation of mammary ducts 2. Enlarge breasts at puberty 3. Antagonize milk-producing effect of prolactin	1. Increases growth of breast lobules and alveoli 2. Induces differentiation of ductal tissue

The uterus is **anteflexed** and normal in size without masses or tenderness.

10- a. What is the normal position of the uterus?

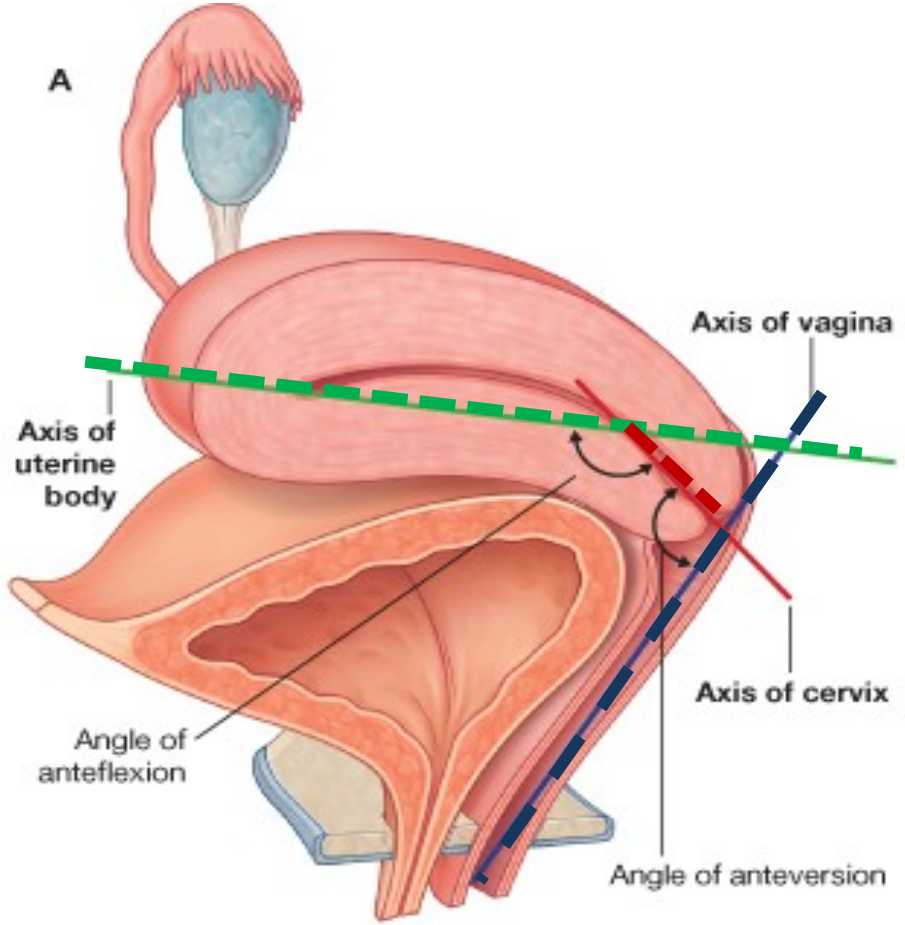
b. What are the factors that keep the uterus in its position?

a. What is the normal position of the uterus?

Anteverted & anteflexed

- **Angle of anteVersion: between longitudinal axis of uterus & axis of Vagina (90)**

- **Angle of anteflexion: between body of uterus and cervix at level of internal os (170) (body is bent forwards on cervix)**



b. What are the factors that keep the uterus in its position?

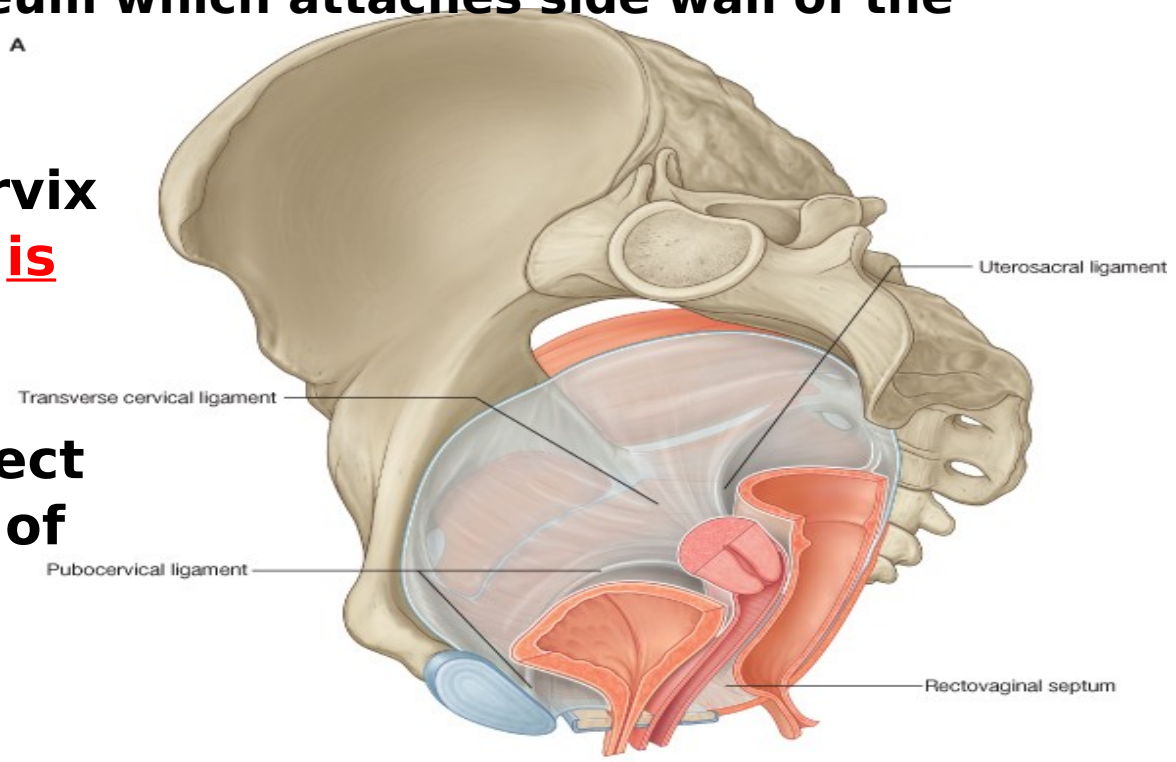
- A number of structures help to maintain the normal position of the uterus. These include the pelvic diaphragm (pubovaginalis part of levator ani), condensations of pelvic fascia & to a lesser extent some peritoneal attachments.

- Pubovaginalis & the perineal body with its inserted muscles support the vagina & hold the cervix up. If pubovaginalis or perineal body are stretched or damaged during childbirth □ vaginal prolapse/

Peritoneal ligaments (Have minimal role in uterine support)

- ***Anterior ligament:*** **fold of peritoneum extends from anterior surface of uterus at junction of body & cervix to upper surface of urinary bladder**
- ***Posterior ligament:*** **fold of peritoneum extends from front of rectum to posterior vaginal fornix & superior to uterus**
- ***Broad Ligament:*** **a lax double fold of peritoneum which attaches side wall of the uterus to side wall of pelvis .**

Fibro-muscular ligaments



1-Transverse cervical: **From side of cervix & upper part of vagina to side of pelvis & is the main support of uterus**

2- Uterosacral: **from posterolateral aspect of cervix across side of rectum to middle of sacrum pull cervix backwards against forward pull of round ligament of uterus**

3- Pubocervical: **From cervix across**

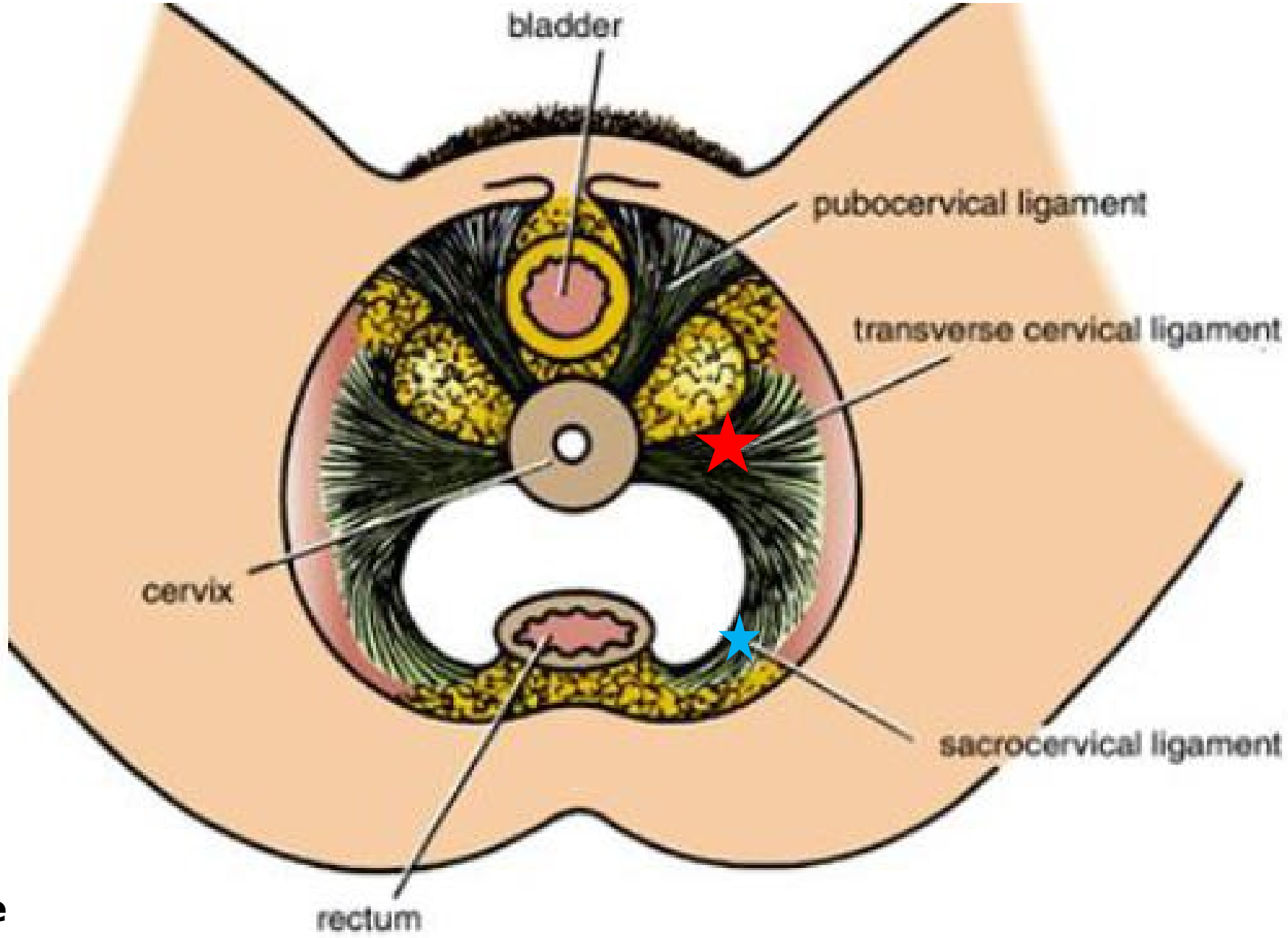
- **These 3 fibromuscular ligaments are condensations of extraperitoneal tissue**

(pelvic fascia) which contain some visceral muscle fibers.

- **The transverse cervical ligament**

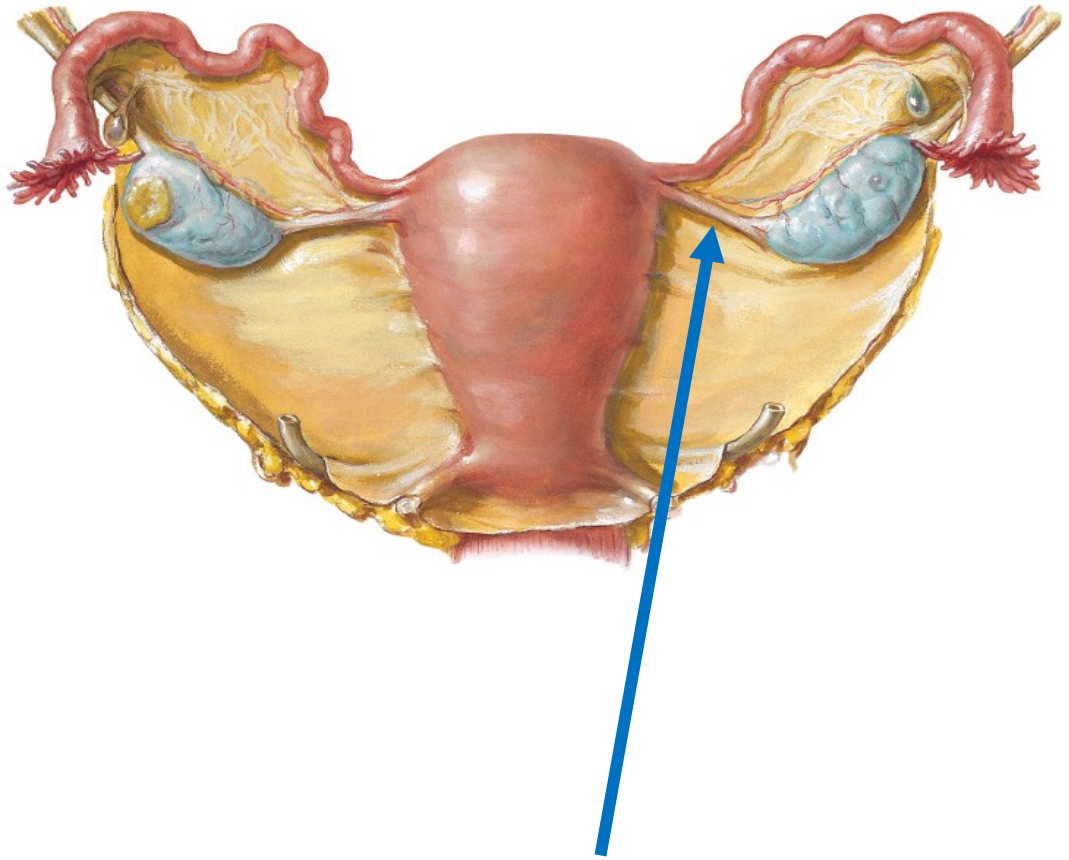
(Mackenrodt's ligament) ⇨ lateral stability to the cervix

- **The uterosacral (sacrocervical) ligaments ⇨ keep the cervix braced backwards against the forward pull of the round ligament of**



4- Ligaments of ovary:

Extend from posterior surface of uterus below and behind uterine tube to the uterine end of ovary



5- Round ligament of uterus:

Extends below and in front uterotubal junction

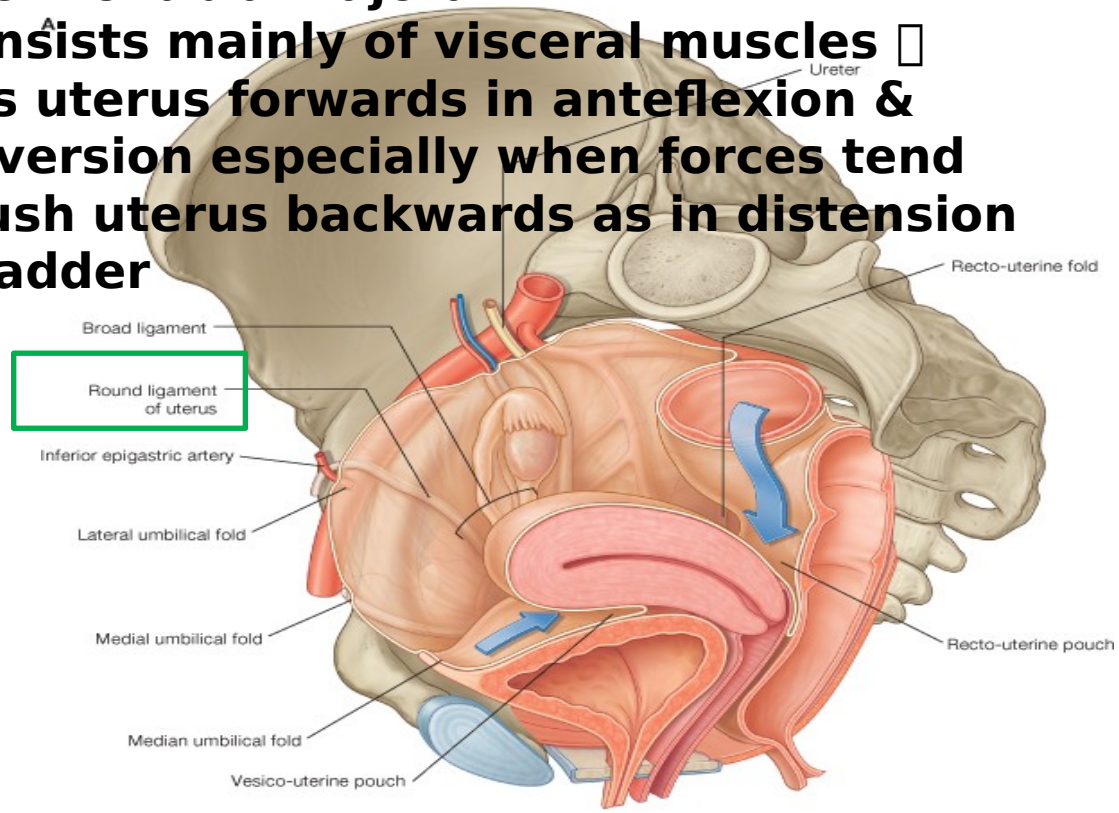
- **Raises a ridge on lower surface of broad ligament**

→ **Crosses on lateral wall of pelvis**

- **Hooks around inferior epigastric artery**
- **Passes in deep inguinal ring& inguinal canal**

→ **Attach to labia majora**

→ **It consists mainly of visceral muscles holds uterus forwards in anteflexion & anteversion especially when forces tend to push uterus backwards as in distension of bladder**



11- How could you investigate this couple?

Investigations

- Male investigations

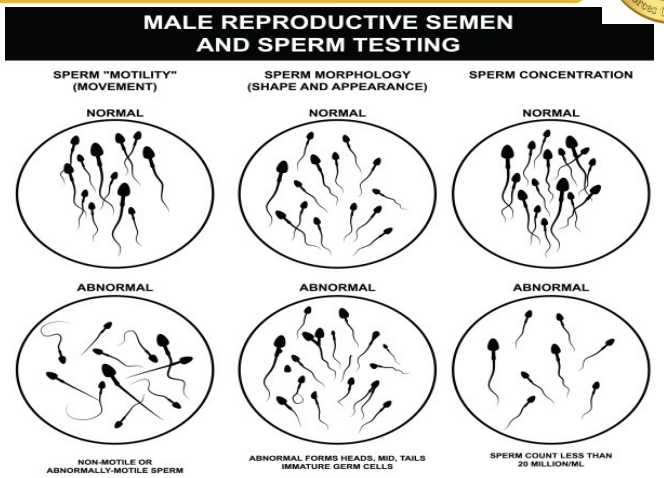
Semen analysis

- Female investigations

1. serum prolactin
2. FSH , LH
3. TSH , T3 , T4

Welcome Back

I want to get pregnant

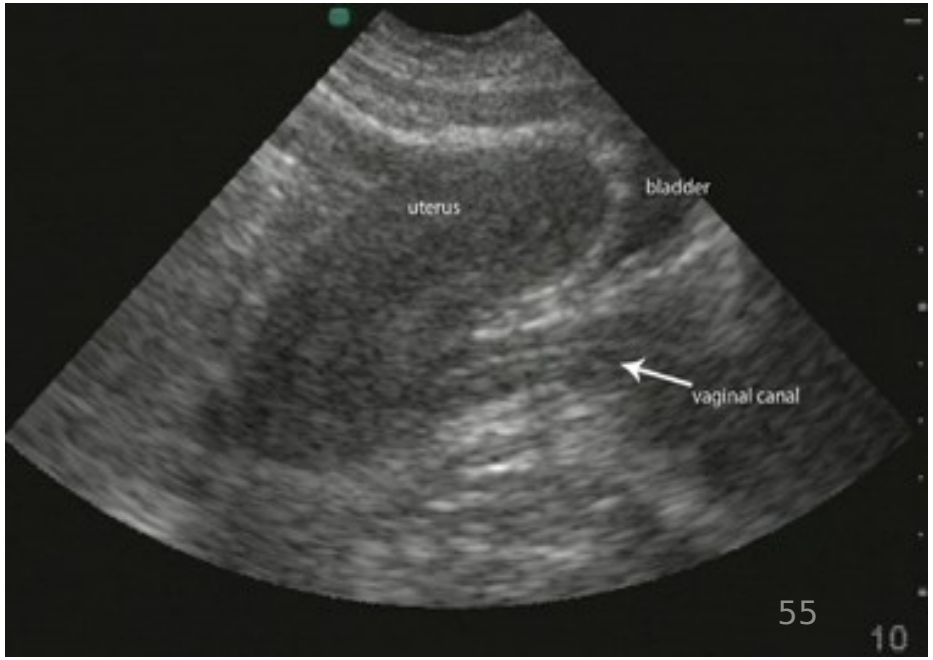


The doctor asked Roshdy to undergo **semen analysis.**

The doctor asked Laila to do serum

- Prolactin,
- FSH and LH levels
- TSH, T3, T4

The doctor asked for **pelvic ultrasonography**



I want to get pregnant

Results showed:

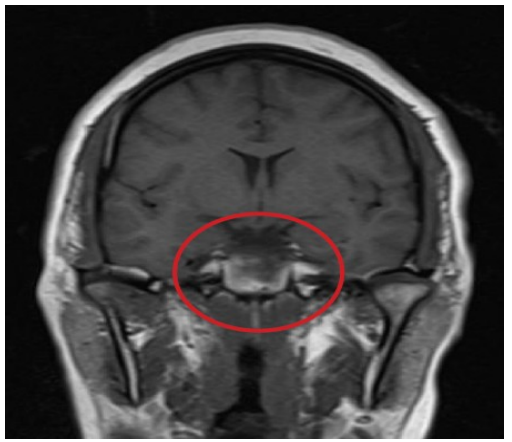
Total sperm number: 5 million spermatozoa per ejaculate

Total motility: progressive motility 30% or more motile

Laila lab results:

- Prolactin: increased 200ng/ml
- FSH and LH levels: normal
- TSH, T3, T4: normal

The doctor asked for CT for Laila. She was found to have microadenoma and was given Dostinex



Discussion

The doctor asked Laila to do serum

- Prolactin,
- FSH and LH levels
- TSH, T3, T4

What is the significance of these hormones?

Significance of hormones

- Serum prolactin

according to our case this mostly a case of anovulation due to hyperprolactinemia represented by galactorrhea

- FSH , LH

as these are the dominant hormones responsible for regulation of the ovarian cycle

- TSH , T3 , T4

as any abnormality in thyroid hormones levels could affect menstruation and cause oligomenorrhea or menorrhagia

How could you manage this case?

Management

The patient was given Dostinex (cabergoline) which is dopamine agonist to control hyperprolactinemia

12- What is the mechanism of action of dostinex?

Laila was given **Cabergoline** (Dostinex)

What is the mechanism of action of **cabergoline** (Dostinex)?

- **Cabergoline (Dostinex) is an ergot derivative**

It is a long-acting dopamine D2 receptors agonist inhibits prolactin release.

Although Bromocriptine is also a dopamine receptor agonist and can also inhibit prolactin release

But cabergoline is the drug of choice.

Why?

Bromocriptine:

- **Once daily**
- **Less potent**
- **More side effects**

Cabergoline :

- **Twice weekly**
- **More potent**
- **Less side effects**

N. B:

Cabergoline is effective in many cases of pituitary tumors resistant to

Take home message

Basic Work-up for Infertility

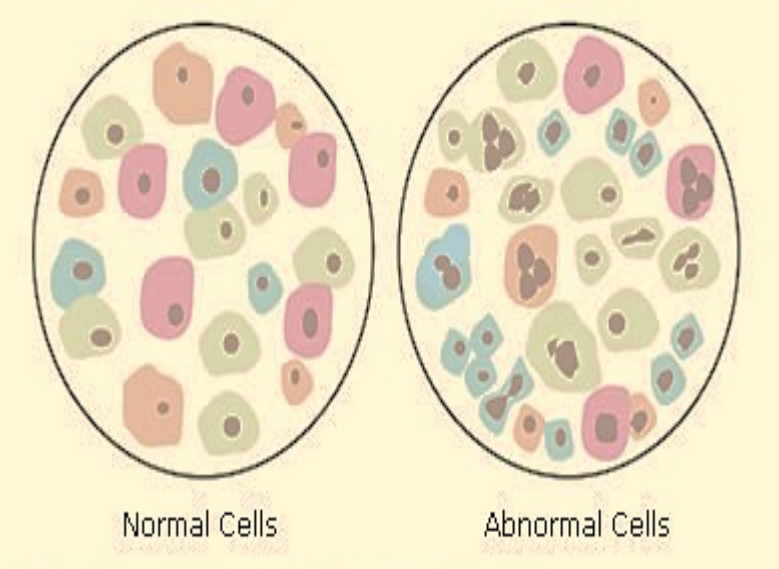
- **Semen analysis:**
  - semen volume: 1.5ml or more
  - pH: 7.2 or more
  - **sperm concentration:** 15 million spermatozoa per ml or more
  - **total sperm number:** 39 million spermatozoa per ejaculate or more
  - **total motility:** 40% or more motile or 32% or more with progressive motility
  - vitality: 58% or more live spermatozoa
  - **sperm morphology** (percentage of normal forms): 4% or more


Thank
you

Laila has no history of sexual transmitted diseases and **no abnormal Paps**.

What is the importance of Paps?

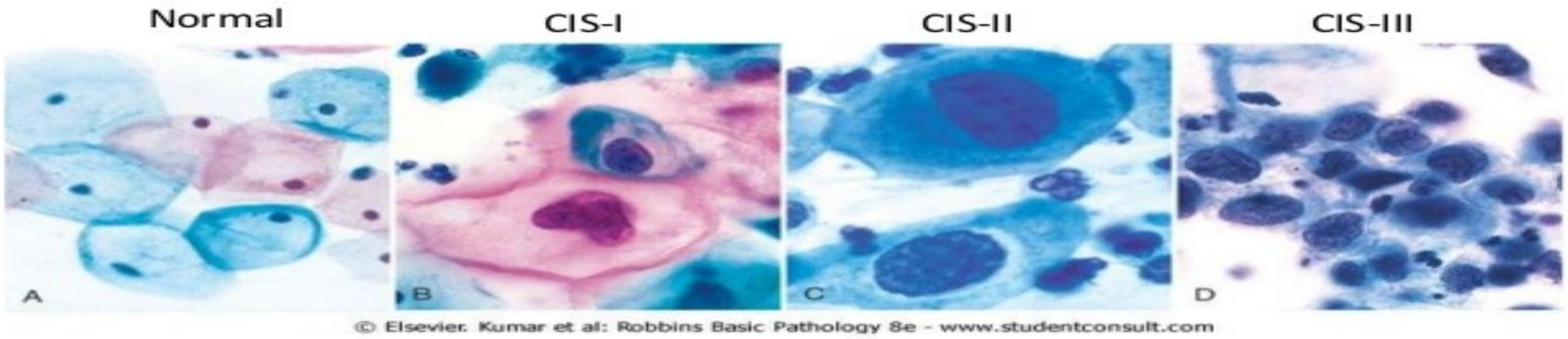
Results of Pap Smear



Normal: no abnormal cells were seen.

Atypical cells: the cells are not clearly normal or abnormal. This may be due to HPV, vaginal infections, or a processing issue in the lab.

Abnormal: the cells are precancerous, or dysplastic.



There is Progressive reduction of size of Cytoplasm, and increase in Nuclear Cytoplasm Ratio as the grade of lesion progresses, which reflects there is loss of cellular differentiation on the surface of cervical lesion